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Pulmonary Complications of Drug Abuse

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Complications resulting from drug abuse more frequently affect the lung than any other organ. The spectrum of pulmonary complications associated with drug abuse is wide. The current practice of using mixtures of drugs is mainly responsible for the increase in pulmonary complications. The chief complications observed in a series of 241 drug abuse patients were aspiration pneumonitis (12.9 percent), pulmonary edema (10.0 percent), and pneumonia (7.5 percent).

DRUG ABUSE frequently results in pulmonary complications of well defined categories. The heroin addict should be considered as part of multiple drug abuse. The drug the patient abuses may contain varying amounts of different active drugs as well as toxic adulterants.[1] The pattern of drug abuse keeps changing as the list of drugs associated with drug abuse constantly expands.[2] The more common drugs observed in the series herein reported includes the congeners of heroin, barbiturates, amphetamines, cocaine, cannabis, and ethanol. Adverse reactions also occur from a loss of opiate tolerance, nonuniformity in drug potency, effect of potentiating drug mixtures, contaminants, and infections due to nonsterile injections.

At the Los Angeles County-University of Southern California Medical Center, there were 264 admissions for heroin-related drug abuse during the period 1971-1972. 241 patients were admitted for pulmonary complications; 23 patients were admitted for heroin drug withdrawal or nonpulmonary complications. The pulmonary complications consisted of clearly defined entities and are

TABLE 1.—*Pulmonary Complications Associated with Drug Abuse (241 Patients)*

	Number of Patients	*Percent*
Overdose, coma, and respiratory depression	137	56.8
Pulmonary edema	24	10.0
Pneumonia	18	7.5
Aspiration pneumonitis	31	12.9
Atelectasis	6	2.5
Septic pulmonary emboli	11	4.6
Lung abscess	12	5.0
Pulmonary fibrosis: Pulmonary vascular talc granulomatosis	2	.8

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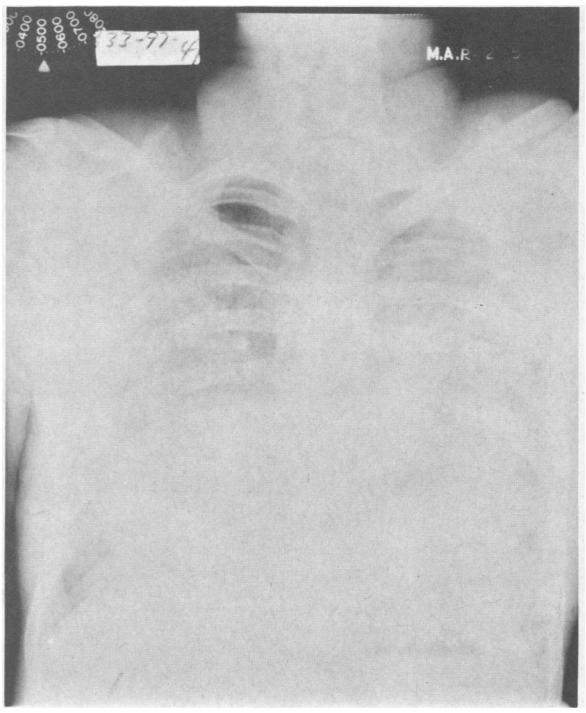

Figure 1.—(Case 1) Pulmonary edema (diffuse and confluent alveolar infiltrates).

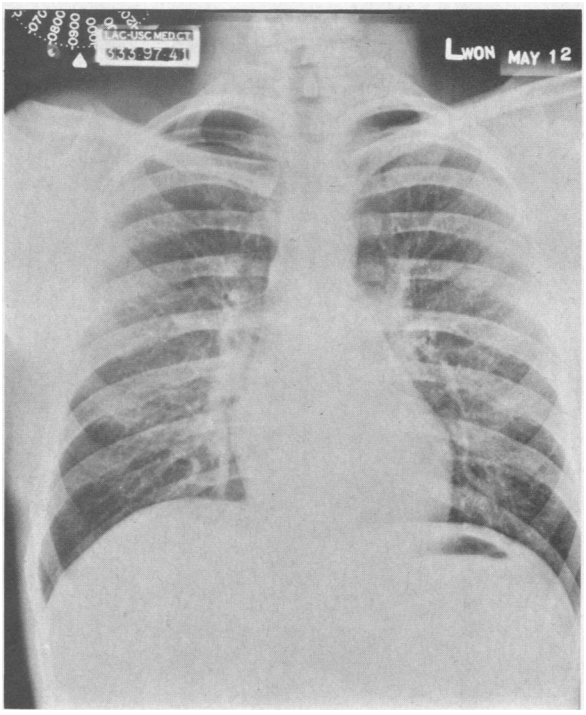

Figure 2.—(Case 1) Chest film showing complete clearing of pulmonary edema.

listed in Table 1. Illustrative cases will describe these complications.

Overdose, coma, and respiratory depression

Patients admitted for drug overdose, coma, and respiratory depression were usually in stage 1 or stage 2 coma and retained good cough and gag reflexes. These patients were given oxygen by Ventimask® (35 percent). Arterial blood specimens were immediately collected for determinations of blood gases, for narcotic and non-narcotic screens, and for glucose and creatinine determinations. Patients with weak or absent gag and cough reflexes were intubated and gastric lavage was instituted. Mechanical ventilation was administered until the blood gases were at a safe level. Urine specimens were obtained for narcotic and non-narcotic screens and routine urinalysis. A chest x-ray film was routinely taken. The majority of these patients responded within 24 hours and were discharged.

Pulmonary edema

Pulmonary edema is one of the critical complications of heroin overdose and may result in sudden death or necessity for admission to hospital. A white or pink froth is frequently found in the mouth or nose; respiratory depression, cyanosis, and constricted pupils are usually evident. Moist rales, rhonchi and wheezes may be heard over the chest. The systolic blood pressure is variable, but is seldom below 90 mm of mercury. Needle tracks should be searched for, and occasionally they are found in bizarre locations.

CASE 1.—A 24-year-old man was admitted to the emergency room comatose and cyanotic, with a bloody froth coming from his mouth. The patient had been drinking ethanol and had taken a "fix" of heroin intravenously just before lapsing into unconsciousness. He had also been a regular marijuana smoker and had taken amphetamines at various times. Blood pressure was 100/70 mm of mercury and body temperature 96°F. Pin point pupils were present; gag and cough reflexes were absent. Moist rales and rhonchi were heard over his chest. The arterial blood gases (room air) were pO_2 26 mm Hg, pCO_2 47 mm Hg, pH 7.25, HCO_3 18 mEq/L. Narcotics and related bases were detected in a urine sample. The chest x-ray film showed diffuse and confluent alveolar infiltrates (Figure 1).

The patient was intubated and attached to a ventilator with an oxygen concentration of 100 percent. Naloxone (Narcan®) 0.4 mg and furosemide (Lasix®) 40 mg were administered intra-

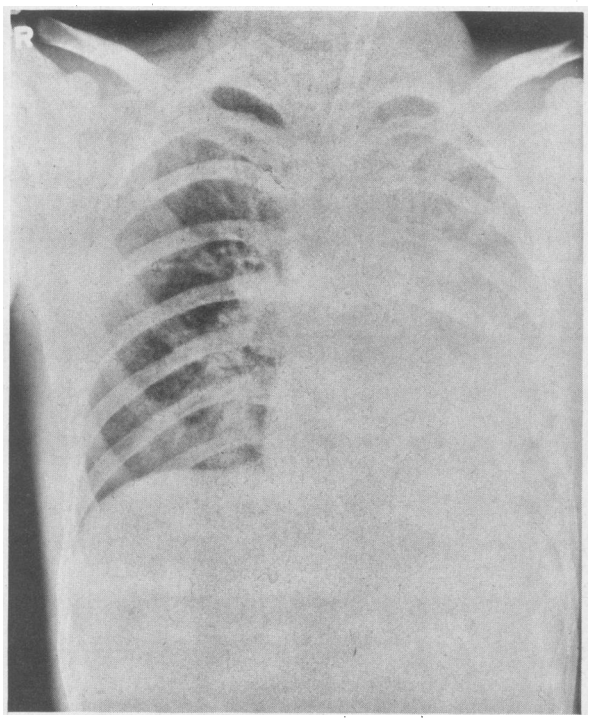

Figure 3.—(Case 2) Pneumonic consolidation in the left lung.

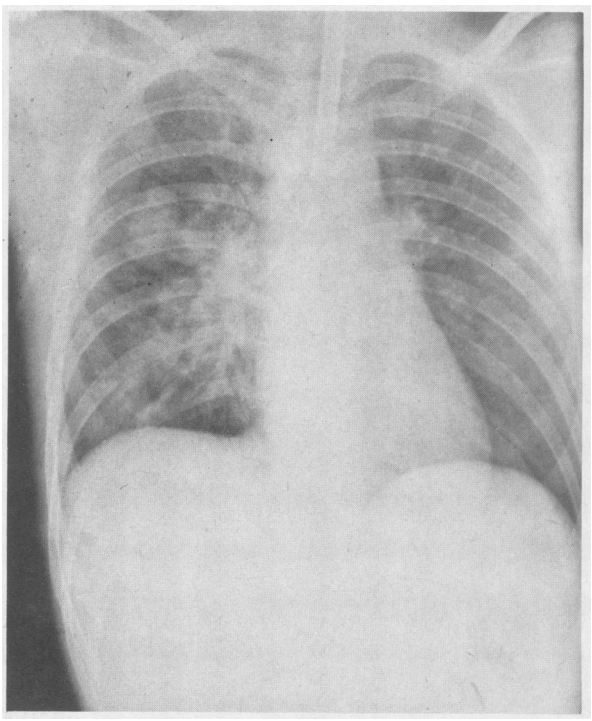

Figure 4.—(Case 3) Aspiration pneumonitis of right lower lobe.

venously. Steroids were given for 48 hours. An x-ray film of the chest five days later showed complete clearing of the pulmonary edema (Figure 2).

Pneumonia

Pneumonia associated with drug abuse may be due to direct bacterial invasion or may follow pulmonary edema or a pulmonary infarct.

CASE 2.—An 18-year-old comatose patient was admitted to the emergency room. He had been found at a party with heroin needles, barbiturate tablets, and amphetamines in his pockets. Reflexes were absent, the pupils were constricted, and there were multiple needle scratches over the extremities. The blood pressure was 100/60 mm of mercury, the pulse rate 100 and the respiratory rate 20. Diffuse rhonchi were heard over the left side of the chest. Sputum culture showed numerous Pneumococci and Klebsiella organisms. Leukocytes numbered 20,000 per cu mm. A culture of blood was negative. A blood specimen showed the presence of long-acting barbiturates, 17 mg per 100 ml, and a urine specimen was positive for narcotic bases. The arterial blood gases (room air) were pO_2 34 and pCO_2 49 mm of mercury, pH 7.26 and T_{40} 22. An x-ray film showed a pneumonic consolidation of the left lung (Figure 3). The patient was intubated and attached to a ventilator. Nalorphine (Nalline®) 10 mg was given intravenously. Cephalothin and kanamycin were given every six hours. The patient recovered and was discharged two weeks after admission.

Aspiration pneumonitis

Vomiting and aspiration of gastric contents into the lungs are often associated with drug overdose. Milk is frequently found in the aspirated material. Milk is sometimes given orally or intravenously by heroin users in the mistaken belief it is a resuscitative procedure. The increasing hypoxemia that follows aspiration is indicative of aspiration pneumonitis.

CASE 3.—A 19-year-old man was admitted to the emergency room in a semicomatose state. He was a known chronic heroin and barbiturate user and, while being transported to the hospital he had aspirated vomitus.

On admission to the ward, the patient was awake and complained of pain in the right side of the chest. He had fever and a rapid pulse. Short-acting barbiturates, 1.8 mg per 100 ml were found in the blood and narcotic bases were detected in the urine. A chest x-ray film showed a patchy infiltrate extending from the hilum to the right lower lobe (Figure 4). Bronchoscopic exam-

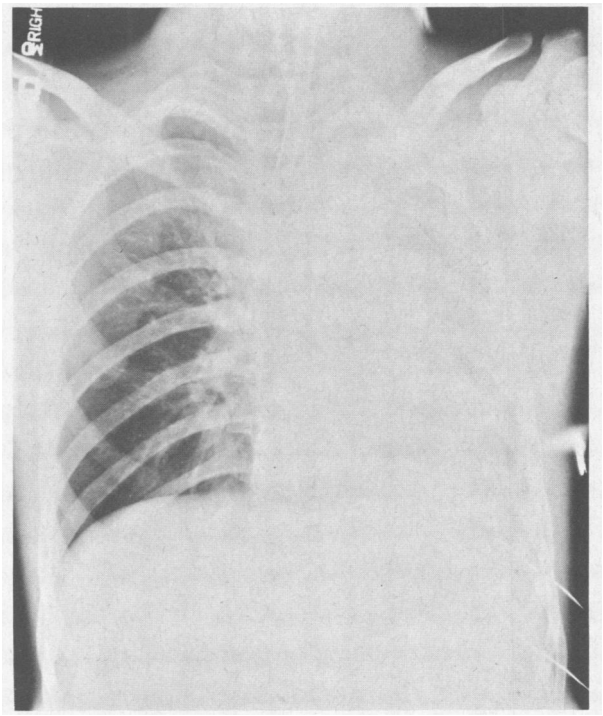

Figure 5.—(Case 4) Chest film showing atelectasis of left lung.

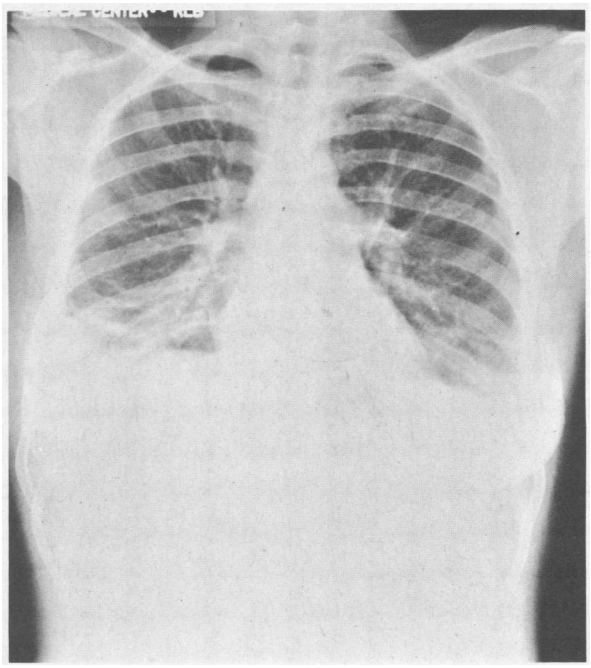

Figure 6.—(Case 5) Chest film showing a round infiltrate in the right costophrenic sulcus with an area of discoid atelectasis proximal to it, consistent with a pulmonary infarct.

ination with lavage was carried out. The right main bronchus was inflamed and moderately edematous. Discolored mucoid material obtained from the bronchus had a pH of 5. A broad spectrum antibiotic and steroids were administered for 72 hours. X-ray studies showed complete resolution of the pulmonary density after five days.

Atelectasis

Atelectasis frequently follows drug overdose. The degree of collapse is variable, ranging from segmental to total involvement of one lung. Atelectasis may result from the retention of secretions due to an ineffectual cough reflex, or may follow the aspiration of gastric contents into the tracheobronchial tree. When atelectasis follows the aspiration of gastric contents, the right lower lobe is usually involved. The posterior segments of the upper lobes and the superior basal segments of the lower lobes are prone to atelectasis due to the gravitational spread of secretions into the dependent areas of the lung.

CASE 4.—An 18-year-old man, a heroin addict, was admitted to the emergency room in a comatose state. He was cyanotic and respiration was depressed. The blood showed long-acting barbiturates, 15 mg per 100 ml, and narcotic bases were detected in the urine. The left hemithorax was dull on percussion, and rhonchi and wheezes were heard over the entire area. A chest x-ray film showed opacification of the left lung with the heart shadow and mediastinum shifted to the left hemithorax (Figure 5). At bronchoscopy, a large viscid mucous plug was suctioned from the left main bronchus. The left lung subsequently re-expanded.

Septic pulmonary emboli

Septic pulmonary emboli associated with drug abuse have their origin from an infected subcutaneous, intramuscular, or intravenous injection site. An alternate source for emboli is tricuspid endocarditis. The embolic material from the injection site and that from right heart endocarditis or tricuspid valvulitis is usually bacterial.

CASE 5.—(Septic pulmonary embolus from a peripheral site.) A 26-year-old woman, a known heroin addict, was admitted to the ward as a transfer from another hospital. On admission, numerous infected needle tracks were noted over both antecubital areas and legs. The temperature was elevated, the pulse was 110, the blood pressure 144/60 mm of mercury. No abnormalities were noted on auscultation of the heart. Coarse rales were present over the right lower hemithorax. The leukocyte count was 24,200 per cu mm. A

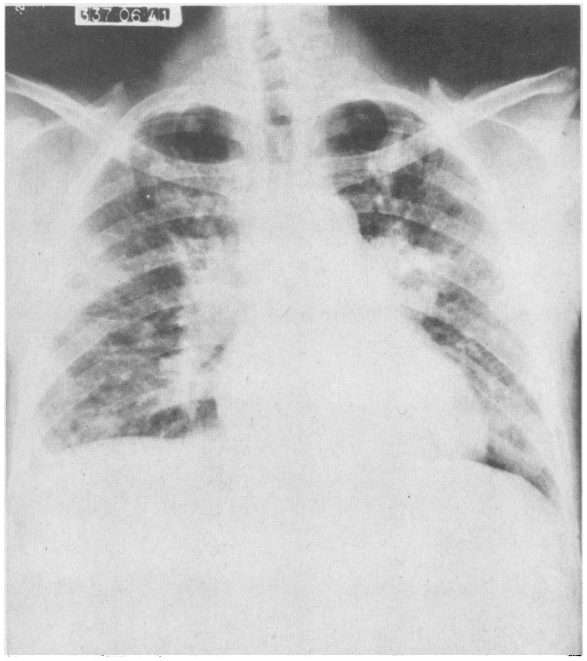

Figure 7.—(Case 6) Patchy infiltrates in both bases, with central lucencies suggestive of cavitary pulmonary infarcts.

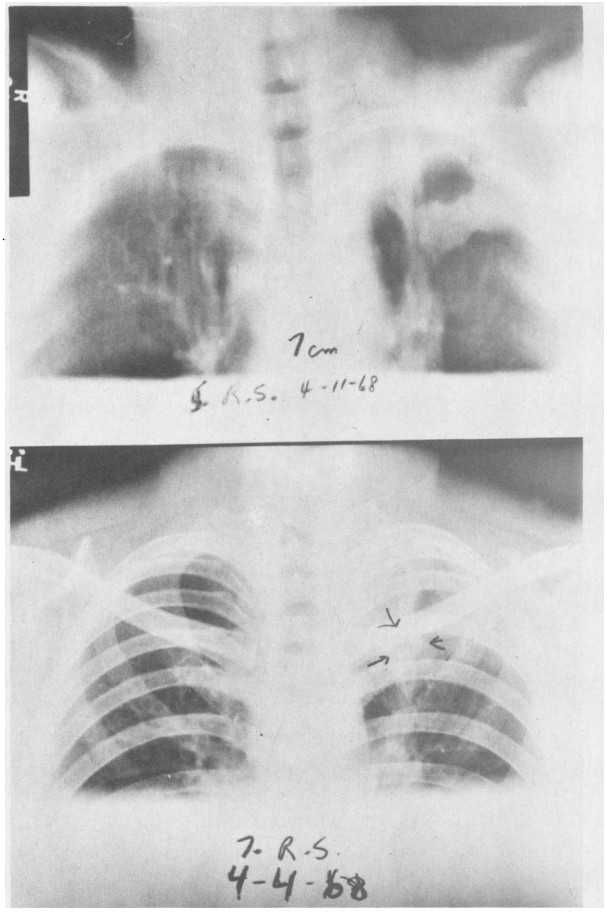

Figure 8.—(Case 7) Chest film and tomogram showing a thick-walled cavity in the left upper lobe.

blood culture showed hemolytic Staphylococcus aureus, coagulase positive, that was sensitive to methicillin. The arterial blood gases (room air) were pO_2 43 mm and pCO_2 29 mm of mercury, and the pH was 7.54. An x-ray film of the chest showed a round, opaque infiltrate in the right costophrenic sulcus with an adjacent area of discoid atelectasis (Figure 6). The infiltrate was consistent with a septic infarct. The patient responded to methicillin and supportive treatment, with resolution of the infiltrate after three weeks.

CASE 6.—(Septic pulmonary embolus from tricuspid valvulitis.) A 24-year-old man was admitted to the hospital with chills, elevated temperature, anorexia, and left lower chest pain of a week's duration. He had been injecting heroin intravenously for the past seven years, the last injection had occurred several days before the present illness. On examination, old and new needle tracks were noted over the antecubital areas. A grade III/VI systolic murmur was heard at the lower sternal border. A systolic ejection click was heard over the pulmonic area as well as a diastolic gallop. Coarse rales were heard over the left lung base. Hematuria was present and blood cultures repeatedly grew Staphylococcus albus and aureus, coagulase positive. A chest x-ray film showed patchy infiltrates in both lung bases with central lucency, suggestive of cavitary pulmonary infarcts (Figure 7). The patient responded to cephalothin therapy with complete resolution of the pulmonary lesions. Extended cephalothin therapy was continued to control the tricuspid valvulitis.

Lung abscess

Lung abscess is a frequent complication of drug addicts,[3] and may be secondary to pneumonia, aspiration pneumonitis or necrotizing pulmonary infarcts. Aerobic microorganisms are chiefly the predominant bacterial agent involved, but anaerobic organisms are often implicated.

CASE 7.—A 30-year-old man was admitted to the hospital with complaint of sharp pain in the left anterior chest region and a productive cough with bloody sputum. He admitted to being a heroin user. On examination, old and new needle tracks were noted over both antecubital areas. Rhonchi and crepitant rales were heard over the left upper chest. Sputum culture showed Pseudomonas and Streptococcus viridans (alpha) orga-

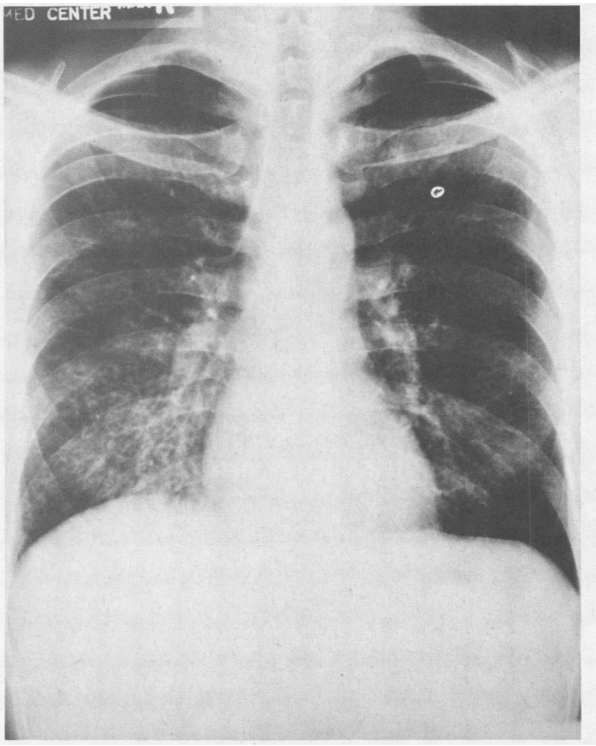

Figure 9.—(Case 8) Interstitial nodulo-reticular infiltration in the lower lobes of both lungs.

nisms. A chest x-ray film and tomograms showed a thick-walled cavity in the left upper lobe (Figure 8). With persistent postural drainage, physical therapy, and appropriate antibiotics, supplemented with repeated bronchoscopic drainage, complete resolution of the abscess occurred.

Drug abuse associated with pulmonary fibrosis and pulmonary vascular talc granulomatosis

Pulmonary fibrosis and pulmonary vascular talc granulomatosis are the sequelae of intravenously injected particulates from material used to filter dissolved heroin, or may be the result of intravenous mixtures of dissolved tablets intended for oral consumption.

CASE 8.—A 33-year-old man was admitted to the hospital with complaint of a cough and chest pain. He had been a heroin addict and had on frequent occasions intravenously injected mixtures of heroin and dissolved barbiturate or methylphenidate (Ritalin®) tablets. On examination, needle tracks were observed in several locations. Coarse inspiratory rales were heard over the right hemithorax. A chest x-ray film showed an interstitial, nodular-reticular infiltration in the lower lobes of both lungs (Figure 9). On polarized microscopic examination, a trephine (drill) biopsy specimen from the right lower lobe showed arteritis, granulomas and talc crystals in the alveolar and perialveolar areas (Figure 10).

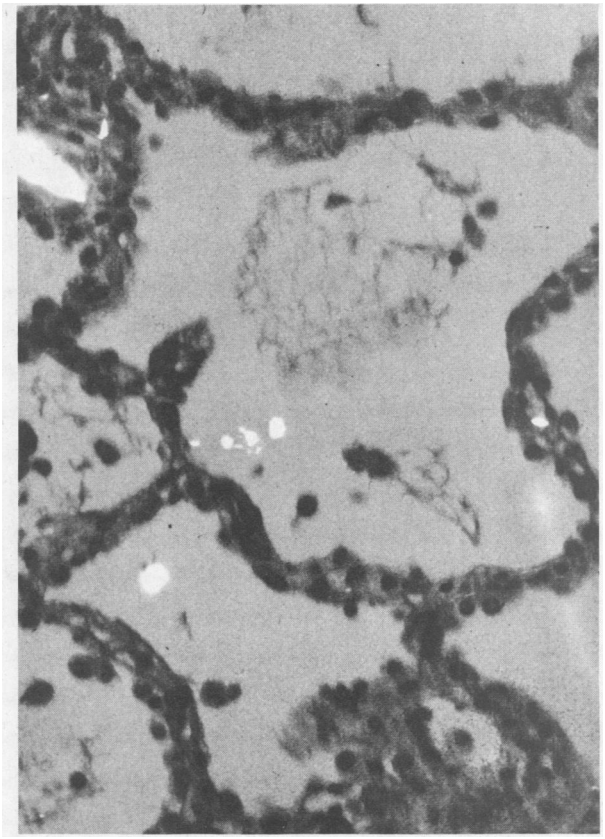

Figure 10.—(Case 8) Biopsy specimen of the right lower lobe showing granulomas and talc crystals by polarized light microscopy.

Discussion

Of all the various congeners of heroin that are taken illicitly—morphine, codeine, pantopon and methadone—heroin is the most widely used. The popularity of heroin apparently is related to the easy availability of this drug, particularly in large cities. In heavily populated urban areas, contacts are quickly established to negotiate for the purchase of heroin. Many of the untoward reactions may be traced to this stage of heroin procurement. The street vendor or pusher reduces the potency of the drug by adding various agents—milk sugar, lactose or quinine. The potency is seldom uniform and overdose frequently results from exceeding the user's tolerance. Moreover, sanitary precautions are seldom observed in the "cutting" process, thus increasing the likelihood of septic contaminants. In addition, other agents that are used to cut the drug may have deleterious effects on the

user, notably corn starch, mannite, baking soda, and talc.

Contributing to the increasing incidence of pulmonary complications associated with the heroin drugs is the present vogue of injecting potentiating combinations of drugs and the concomitant use of ethanol. The following intravenous mixtures have been observed in this series: Heroin combined with dissolved oral tablets or capsules containing such drugs as methadone, barbiturates, amphetamines, glutethimide, phenmetrazine hydrochloride, methylphenidate hydrochloride and phencyclidine hydrochloride.

Another important factor in precipitating drug overdose is the loss of tolerance in the addict following a period of withdrawal treatment or abstention; the dose he was previously accustomed to, then may become an overdose.

Complications also occur from the bizarre methods of illicit drug administration. The more common method of taking heroin is the intravenous route ("mainliner"); however, the injection site is seldom made sterile, thereby providing a nidus for hematogenous infections. Heroin is often injected into the skin either subcutaneously or through clothing ("skin popper"). This kind of administration leads to the formation of chronic subcutaneous abscesses, cellulitis, and granulomas. Hepatitis, tetanus, and malaria have also resulted from indiscriminate, unsterile heroin-drug injections. The inhalation of heroin ("snorter") and the smoking of heroin have been associated with overdose and pulmonary edema. Awareness of these forms of administration as well as of the sublingual injection method is important, since needle tracts or skin stigmata may not be evident as diagnostic clues of drug abuse.

The onset of pulmonary edema following heroin-drug overdose is instantaneous in most cases, although in some cases the edema does not appear until 24 to 48 hours after hospital admission and occasionally may develop as the patient emerges from coma. Changes in serial chest x-ray films and sequential arterial blood gases are reliable indicators of pulmonary edema. Alveolar infiltrates that become diffusely confluent with absence of cardiac enlargement and venous congestion would tend to preclude pulmonary edema of cardiac origin. The abrupt appearance of pulmonary edema in a young person without underlying cardiac disease usually is indicative of heroin overdose.

Coma and pulmonary edema may be produced by overdose with a large number of narcotic agents. These drugs include heroin, morphine, methadone, meperidine, hydromorphone, codeine, oxycodone, hydrocodone, diphenoxylate, propoxyphene, and pentazocine. Most addicts prefer heroin.[4]

Narcotic antagonists are important adjuncts in the therapy of heroin and narcotic related overdose. Nalorphine and naloxone are the two most widely used narcotic antagonists; the latter is the drug of choice. Naloxone does not have the agonistic effects induced by nalorphine, which are similar to those of narcotics, namely, respiratory depression, miosis and depression of certain reflexes.[5] Moreover, naloxone is not effective in reversing the depressive effects of non-narcotic agents, barbiturates and phenothiazine tranquilizers; hence it may be utilized as a diagnostic test to exclude suspected opiate overdose. Narcotic antagonists can precipitate pronounced withdrawal symptoms in narcotic addicts and may require prompt counteractive measures.

The pathogenesis of heroin-induced pulmonary edema remains unclear; however, various hypotheses have been advanced. Hypersensitivity and anaphylaxis to the injected material have been suggested as etiologic factors.[6] This theory is plausible to account for the immediate deaths and pulmonary edema from heroin overdose, but does not readily explain the delayed subsequent onset of pulmonary edema. The similarity of heroin pulmonary edema to the pulmonary edema that follows neurogenic disorders such as cerebral tumor, trauma and vascular accidents has led to speculation that the central nervous system is implicated in heroin pulmonary edema.[7] However, the lack of spinal fluid abnormalities in these cases appears to negate a neurogenic association. Adulterant agents commonly used to "cut" the purity of heroin have been suspect of initiating pulmonary edema, either by a toxic or an allergic effect. Quinine, a common "cutting" agent, could have a potentially deleterious action on the heart,[8] but these reactions are not observed with other adulterants. A current theory as to the cause of heroin pulmonary edema underlines the factors of hypoxia, alveolar hypoventilation and increased capillary permeability.[9] The mechanism is analogous to that of high altitude pulmonary edema: Anoxia, depressed respiration, increased capillary

permeability, and extravasation of fluid leading to pulmonary edema.[10] A recent study by Katz and associates[11] suggests that heroin pulmonary edema may be the result of increased capillary permeability with the extravasation of serum into the alveoli, directly related to the opiate and not necessarily due to hypoxia. The pulmonary edema fluid has been reported to have a high protein concentration characteristic of serum.[11,12]

The sequential pathologic features of acute heroin pulmonary edema have been well documented. From cases in which the interval between the intravenous injection and death is known, the following conclusions have been derived.[13] When the time between the intravenous injection of the narcotic and death is within three hours, the lungs at autopsy have a boggy and congested appearance, and numerous foci of atelectasis and emphysema are found. When the interval is three to twelve hours between the lethal injection and death, "narcotic lungs" are noted at autopsy. The lungs are edematous, with a whitish froth filling the air passages. The lobular markings are outlined and patchy areas of emphysema and atelectasis are found in the anterior areas. The alveoli contain fibrin and a hyaline membrane is found in many of the alveoli. After 24 hours, the lungs have a meaty, reddish, granular appearance suggestive of confluent lobular pneumonia.

The physiologic findings of heroin pulmonary edema characteristically represent the features of respiratory depression—decreased ventilation, hypoxemia, hypercapnia, elevation of the alveolar-arterial oxygen gradient and arterial oxygen desaturation. A combined respiratory and metabolic acidosis is frequently associated with heroin pulmonary edema.[14] Pulmonary function tests show a pronounced reduction in total lung capacity, in vital capacity, and in 1-second forced expired volume. The carbon monoxide diffusing capacity is also significantly reduced. Functional impairment may persist for ten to twelve weeks.[15]

Pneumonia appears with greater frequency than might be suspected in patients admitted for drug overdose. Louria and co-workers observed that the susceptibility to pneumonia was related to the duration of heroin use.[16]

The occurrence of aspiration of gastric contents is difficult to ascertain in the absence of residual gastric particulates in the pharynx or around the mouth and nose. Aspiration may be suspected although not yet detectable by chest x-ray or physical findings if significant right to left shunting is present.[17] When the patient is seen shortly after aspiration, bronchoscopic suction and lavage may be helpful, especially if the gastric particulates are large and distributed bilaterally. The availability of the flexible bronchoscope will undoubtedly encourage the more frequent use of this procedure. Steroids and antibiotics are also of benefit in the early stages of aspiration pneumonia.[17,18]

Septic pulmonary emboli linked with intravenous drug abuse usually originate from an area of septic thrombophlebitis in close proximity to an infected injection site, or from the right sided endocarditis. Frequently, septic pulmonary emboli may present as pneumonia with Staphylococcal septicemia.[19] Emboli arising from the tricuspid valve are usually bacterial. The radiologic features of septic pulmonary emboli may vary from small, scattered, consolidated areas simulating bronchopneumonia to round or wedge-shaped opacities.[20] The pulmonary lesions may also be multiple, appearing in one area of the lung and then another.[21] The infarcts may resolve or undergo cavitation and abscess formation. Infrequently, the septic infarct will extend to the pleura, resulting in empyema. With complete resolution of the infarct, the radiologic features may return to normal; occasionally, residual fibrotic, atelectatic areas or pleural thickening persist.

Intravenous multi-drug abuse may result in pulmonary talc granulomatosis. The current trend among drug addicts of combining heroin with dissolved tablets intended for oral use, and injecting these mixtures intravenously, accounts for this manifestation. The more commonly used mixtures include heroin and methylphenidate hydrochloride (Ritalin®), or heroin and dissolved barbiturate or amphetamine tablets. Tablets generally contain a filler substance consisting mainly of talc (magnesium trisilicate) which may produce, when injected intravenously, a granulomatous reaction in the lungs. Often, fibers (from cotton or gauze used to filter the drug mixture) included in the intravenous injection also lodge in the lung. The observed pulmonary granulomas have a characteristic perivascular or intravascular location.[22] Necropsy studies indicate that the larger talc particulates are filtered by the lungs,[23] and they are easily discernible with polarized light microscopy. The chest x-ray films of these patients are suggestive of interstitial pulmonary fibrosis. A reduc-

tion in the carbon monoxide diffusion capacity is found in former addicts and in heroin users with hepatitis. This could be compatible with the possibility that chronic diffusion impairment results from foreign body granulomas in the lung.[24] Talc-induced pulmonary granulomatosis may be instrumental in producing pulmonary hypertension and cor pulmonale.[25]

Pulmonary edema was the major complication in this series. Of 24 patients (10 percent) admitted with pulmonary edema, four died. A higher incidence of pulmonary edema and deaths has been reported in other series. Duberstein and Kaufman[10] noted the ocurrence of pulmonary edema in 71 (48 percent) of 149 patients admitted over a period of 17 months for heroin overdose. Thirteen patients (8.7 percent) died, all 13 had pulmonary edema.

Trade and Generic Names of Drugs

Narcan® ..... naloxone
Nalline® ..... nalorphine
Lasix® ..... furosemide
Ritalin® ..... methylphenidate

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